Anaphylaxis: clinical features and GP’s role in management

Priya Sellaturay BSc, MRCP, Krzysztof Rutkowski MD, MRCP and Shuaib Nasser MA, MD, FRCP

Anaphylaxis can be fatal if not treated promptly and it is important to identify likely triggers and educate patients on the proper use of adrenaline autoinjector. Here, the authors outline the clinical features, acute and long-term treatment and the GP’s role in management.

Anaphylaxis is a severe systemic hypersensitivity reaction that may be life threatening if not treated promptly. According to NICE guidelines anaphylaxis is defined as a ‘rapidly developing, life-threatening problem involving: the airway (pharyngeal or laryngeal oedema) and/or breathing (bronchospasm with tachypnoea) and/or circulation (hypotension and/or tachycardia)’.1

The incidence of an individual having anaphylaxis in England is estimated at around 1 in 1333.1 Approximately 20 people are known to die each year from anaphylaxis, with half the deaths caused by drugs; this is probably an underestimate.2

Anaphylaxis may be IgE mediated (type 1 hypersensitivity) requiring initial sensitisation to an allergen with production of allergen-specific IgE antibodies, and subsequent exposure causing mast-cell degranulation with release of allergic mediators including histamine and tryptase. Anaphylaxis may be also non-IgE mediated, eg with NSAIDs. Both IgE- and non-IgE-mediated reactions result in similar clinical features and therefore the term anaphylaxis rather than anaphylactoid (a term previously used for non-IgE-mediated symptoms) is used throughout.

This article focuses on the clinical features of anaphylaxis, triggers, susceptible groups, and acute and long-term management of patients.

Clinical features
Anaphylaxis can present with a wide range of symptoms and is therefore often difficult to diagnose (see Table 1). Symptoms include life-threatening airway and/or breathing and/or cardiac compromise.3 It occurs acutely and can result in cardiac arrest, particularly if symptoms are prolonged or untreated or if there is a pre-existing coronary compromise.

The onset of symptoms varies depending on the trigger with cardiac arrest reported within five minutes of iv drug administration, 15 minutes after a bee or wasp sting and 30 minutes after food ingestion.2 Skin and mucosal changes are present in more than 80 per cent of cases.3,4 Biphasic anaphylaxis has been reported to occur in between 1 and 23 per cent of cases of anaphylaxis.4,5

The authors outline the clinical features, acute and long-term treatment and the GP’s role in management.
Triggers

Triggers include food (eg nuts, egg, milk, wheat, fish, soya, shellfish, meat, lupin, buckwheat, etc), medication (eg antibiotics, especially penicillins and cephalosporins, NSAIDs, neuromuscular blocking agents and contrast media), insect stings (wasp, bee, hornet, etc), and exertion (with or without food), or maybe idiopathic. 6–18

Food is the most common trigger in children and medication in adults. Peanut is the most common food allergen in the USA, with buckwheat and rice common in Asia and sesame in parts of the Middle East. 6 Some triggers require a co-factor, eg in some people food-induced anaphylaxis only occurs if ingestion is followed by either exercise or an NSAID. Wheat is the commonest food causing food-dependent exercise-induced anaphylaxis but shellfish, tomatoes, peanuts and corn have also been implicated. These foods are normally ingested two to four hours before exercise. 6

Diagnosis

A detailed history establishes the cause of anaphylaxis in most cases. Important features to record include: the time of onset, clinical features, when the drugs were administered in relation to the reaction and to list any foods or drugs taken six hours prior to the episode. 5 It is also important to make note of any stings or bites prior to the reaction and to ask about co-factors such as exercise, infection and exposure to heat or cold. 6

An increase in serum tryptase allows confirmation of anaphylaxis and should be measured soon after emergency medications have been administered. 1,6,14 Where anaphylaxis predominantly involves the airway no increase in tryptase level may be detected. 5,15

The differential diagnosis of anaphylaxis includes: acute asthma, urticaria and angioedema, hyperventilation and panic attack, cardiovascular system pathology (MI, pulmonary embolism), shock (hypovolaemic, cardiogenic, septic), vasovagal reactions and ACE inhibitor angioedema; less frequently: flushing syndromes, including mastocytosis, carcinoid, pheochromocytoma, medullary thyroid carcinoma and red-man syndrome (vancomycin), scombroid fish poisoning, food poisoning, vocal cord dysfunction and hereditary angioedema. Vulnerable groups are listed in Table 2.

Management

First-line treatment

Adrenaline is used first line in the treatment of anaphylaxis. A delay in administering adrenaline can be fatal. Adrenaline is an alpha- and beta-adrenergic agonist. The action on alpha 1-adrenergic receptors vasoconstricts and reduces mucosal oedema. Beta 1-adrenergic activity results in positive inotropic and chronotropic effects increasing the force and rate of cardiac contractions, counteracting the effects of shock.

Adrenaline acts also on beta 2-adrenergic receptors. It relieves bronchoconstriction and reduces mast cell mediator release, thereby improving asthma and urticaria. 7

Adrenaline should be administered intramuscularly into the anterolateral aspect of the middle third of the thigh. This site provides more rapid absorption than an injection into the deltoid. 15 In obese patients the length of the needle needs to be sufficient so that adrenaline is administered into the muscle. 5 The dose of adrenaline differs with age (see Table 3). 5,7,15

As vasodilatation occurs during anaphylaxis, it is important to lie the patient down with legs raised to maintain return of circulation to the vena cava. ‘Empty vena cava syndrome’ with cardiac arrest

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Table 1. Clinical features of anaphylaxis (not all symptoms have to be present at the same time). 1,4,6,7,15,16

<table>
<thead>
<tr>
<th>System</th>
<th>Clinical feature</th>
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<tbody>
<tr>
<td>Cutaneous/mucosal</td>
<td>urticaria, angioedema, erythema, generalised pruritus, pruritus of palms and soles of feet, conjunctivitis</td>
</tr>
<tr>
<td>Respiratory/ENT</td>
<td>wheeze/asthma, laryngeal oedema, stridor, dysphonia, rhinitis, itching of palate/external auditory meatus</td>
</tr>
<tr>
<td>Cardiac</td>
<td>hypotension, loss of consciousness/collapse, syncope/lightheadedness, palpitations/tachycardia, cardiac arrest</td>
</tr>
<tr>
<td>Neurological</td>
<td>sense of doom or extreme anxiety, seizures</td>
</tr>
<tr>
<td>Gastrointestinal/genitourinary</td>
<td>nausea, vomiting, abdominal pain, diarrhoea, faecal/urinary incontinence</td>
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</tbody>
</table>

Table 2. Vulnerable groups to anaphylaxis

- Children
- Adults
- Peanut allergy
- Drug allergy
- Food allergy
- Drug reaction
- Insect bite
- Exercise
- Food ingestion
- Medication
- Angioedema
- Drug allergy
- Allergic reaction
- Drug reaction
- Insect bite
- Exercise
- Food ingestion
- Medication
- Angioedema
**Table 2.** Vulnerable groups

<table>
<thead>
<tr>
<th>Vulnerable Group</th>
<th>Vulnerable Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants/children</td>
<td>Unable to report symptoms or symptoms difficult to interpret as some are physiological (spitting, irritability, crying)</td>
</tr>
<tr>
<td>Teenagers/adolescents</td>
<td>Risk-seeking behaviour/denial of severity of allergy, reluctance to carry/use adrenaline autoinjector</td>
</tr>
<tr>
<td>Elderly</td>
<td>Co-morbidities, visual and memory impairment</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Differential includes: pulmonary embolism, cerebral vascular accident, amniotic fluid embolism, spinal block, haemorrhage, etc. Additional symptoms: vaginal/vulval pruritus and fetal distress/preterm labour. Woman’s health is the priority; adrenaline is safe; fetal monitoring crucial, elevate legs (or position of comfort); left lateral position to decompress inferior vena cava, high-flow O₂, rapid fluid replacement to maintain placental circulation and minimise risk of hypoxic-ischaemic encephalopathy, chest compressions difficult in advanced pregnancy, maternal cardiac arrest/sudden deterioration – emergency caesarean-section</td>
</tr>
<tr>
<td>Other</td>
<td>Mastocytosis and poorly-controlled asthma increase severity of allergic reactions. ACE inhibitors, beta-blockers might reduce efficacy of adrenaline and increase severity of anaphylaxis. Adrenaline interacts with MAOIs, tricyclics and linezolid, leading to an increased risk of arrhythmias and hypertension</td>
</tr>
</tbody>
</table>

**Table 3.** Dose of adrenaline

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose of Intramuscular Adrenaline (0.01mg/kg of 1:1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult over 12 years</td>
<td>0.5ml, 0.3ml, 0.15ml</td>
</tr>
<tr>
<td>6–12 years under 6 years</td>
<td>0.5ml, 0.3ml, 0.15ml</td>
</tr>
</tbody>
</table>

Anaphylaxis can be fatal if not treated promptly. High-flow oxygen and iv fluids should be administered in most cases, particularly if the patient is breathless or hypotensive (see Figure 1).

Beta-blockers may reduce the efficacy of adrenaline and the unopposed effects on α₂-adrenergic receptors can cause hypertension, bradycardia and bronchoconstriction. It may require reversal with glucagon.

**Second-line management**

H₁-antihistamines, eg chlorphenamine, relieve urticaria, angioedema, itching, flushing and rhinoconjunctivitis. Steroids, eg hydrocortisone, may prevent biphasic anaphylaxis and relieve protracted reactions. Both are recommended in every case. A β₂-agonist, eg salbutamol nebulas, can be given if there is evidence of lower airway obstruction.

Second-line treatments should not be substituted for adrenaline and should not delay the administration of adrenaline in anaphylaxis.

**GP’s role in management**

Patients will often present to their GP surgery for acute treatment of anaphylaxis. This should be also seen as an opportunity to document details of the reaction and identify the likely trigger. Blood should be sent for serum tryptase measurement and the time recorded in relation to onset of symptoms. Although serum tryptase does not always increase in anaphylaxis, an acute rise will help to diagnose anaphylaxis. A normal level measured within four hours of the onset of symptoms is extremely helpful and may point to an alternative future line of investigation.

The patient or their carer should be instructed to avoid the likely trigger and an adrenaline autoinjector prescribed in most cases. The technique to use an adrenaline autoinjector should be demonstrated at the point of prescription and again when dispensed by the pharmacist. Too often, patients are discharged from A&E with adrenaline autoinjectors but not shown how to use them.

Patients with drug allergy, including those who experience allergic reactions during general anaesthesia, do not require an adrenaline autoinjector, especially if the drug is easily avoidable. If unsure, provide an adrenaline autoinjector in the interim until reviewed by a specialist.

All patients with suspected anaphylaxis should be referred to a specialist allergy service. This ensures patients are accurately investigated, diagnosed, treated and educated in order to reduce their risk of future anaphylaxis. Patients who have had suspected anaphylaxis during general anaesthesia should be referred by the anaesthetist involved with a clear account of all drugs administered and a copy of the anaesthetic and drug charts along with a copy of the anaesthetist’s notes and results of serum tryptase.

**Conclusion**

Anaphylaxis can be fatal if not treated promptly. Intramuscular adrenaline is first-line treatment in all healthcare settings. A detailed history is crucial in establishing the cause of anaphylaxis. Patients provided with an adrenaline autoinjector should be taught how to use it when prescribed and reinforced by the
Acute management of anaphylaxis

Remove potential trigger, eg stinger, drug
Assess: airway, breathing, circulation, disability, exposure
Administer im adrenaline
Lie on back with legs raised
Give high-flow oxygen
Insert cannula, give iv chlorphenamine and hydrocortisone
If iv access is difficult give im
iv 0.9% normal saline
If wheezy give nebulised salbutamol and adrenaline
Measure serum tryptase (5ml clotted blood) immediately after resuscitation and document time taken, send a sample 1–2hr later and a final sample >24hr later
All children should be admitted under the paediatric team
Adults should be observed for 6–12hr hours
Refer to specialist allergy service

Long-term management of anaphylaxis

Following acute treatment of anaphylaxis
Document time of onset of reaction, clinical features and circumstances immediately before onset
Adrenaline autoinjector
Referral to allergy specialist

Education
Information on clinical features of anaphylaxis and biphasic reactions
Educate on how to treat future reactions
Demonstrate how to use adrenaline autoinjector correctly
Advice on avoiding triggers if known
Information on patient groups

References
1. NICE. Anaphylaxis: assessment to confirm an anaphylactic episode and the decision to refer after emergency treatment for a suspected anaphylactic episode. CG134. December 2011.

Declaration of interests
None to declare.

Dr Sellaturay is allergy specialist registrar, Dr Rutkowski is allergy specialist registrar and Dr Nasser is consultant allergist and associate lecturer, Cambridge University Hospitals NHS Foundation Trust